IN THE UNITED STATES DISTRICT COURT

FOR THE DISTRICT OF DELAWARE

CAREDX, INC., Plaintiff, v. EUROFINS VIRACOR, INC., Defendant, and THE BOARD OF TRUSTEES OF THE LELAND STANFORD JUNIOR UNIVERSITY Nominal Defendant.	)	C.A. No. 19-1804-CFC-CJB

DEFENDANT EUROFINS VIRACOR INC'S CONCISE STATEMT OF FACTS IN SUPPORT OF ITS MOTION FOR SUMMARY JUDGMENT THAT THE ASSERTED CLAIMS OF U.S. PATENT NO. 8,703,652 ARE INVALID UNDER 35 U.S.C. § 101

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	Facts	Evidence
1	U.S. Patent Nos. 8,703,652, 9,845,497, and 10,329,607 ("Patents") share the same written description.	●B0001 ●B0025 ●B0049
2	The earliest claimed priority date on the face of the Patents is November 6, 2009.	●*Id.*
3	Circulating, or cell-free, DNA was first detected in human blood plasma in 1948. Since then, its connection to disease has been established in several areas.	●Decl. ¶¶47-58 ●B0001 at 6:57-8:22 ●B0080-B0081
4	Much of the circulating nucleic acids in blood arise from necrotic or apoptotic cells.	●*Id.*
5	Before November 6, 2009, circulating cell-free nucleic acids were useful for fetal diagnostics, with fetal DNA circulating in maternal blood serving as a marker for gender, rhesus D status, fetal aneuploidy, and sex-linked disorders.	●B0001 at 6:67-8:21 ●Decl. ¶¶52-53, 57, 136-145, 147-156 (citing further evidence).
6	Before November 6, 2009, cell-free DNA was useful in cancer detection and treatment, as the presence of sequences different from a patient's normal genotype can be used to detect cancer.	●B0001 at 6:57-7:36; ●Decl. ¶¶54-58.
7	Donor-specific DNA naturally present in a transplant recipient's plasma can serve as a potential biomarker for the onset of organ rejection or failure.	●B0001 at 5:36-40, 6:67-8:56, 10:45-51, 11:22-31, 13:2-24, 15:12-18, 26:51-53; ●Decl. ¶¶39-51, 136-197 (citing further evidence)

8	Naturally-occurring genetic polymorphisms include single nucleotide polymorphisms (SNPs).	●B0001 at 13:41-44; ●Decl. ¶¶39-46; ●B0075; ●B0574.
9	In humans, SNPs naturally occur at about one base out of 1,000 and there are about 3,000,000 differences between any two individuals.	●Decl. ¶43.
10	The practice of the claims of the Patents employs, unless otherwise indicated, conventional techniques of immunology, biochemistry, chemistry, molecular biology, microbiology, cell biology, genomics and recombinant DNA, which are within the skill of the art as of November 6, 2009.	●B0001 at 5:36-49, 6:57-58, 8:55-60, 9:8-14, 10:11-51, 11:22-31, 13:2-67, 14:29-18:53, 20:31-44, 21:5-9, 23:31-36, 26:47-53; ●Decl. ¶¶67-135, 146-197 (citing further evidence).
11	Obtaining or providing a blood sample could be performed using any technique known in the art by November 6, 2009, including a syringe or other vacuum device.	●B0001 at 6:57-67, 9:4-14, 10:7-12; ●Decl. ¶¶73-77.
12	The Patents do not disclose or claim any nonconventional laboratory techniques for obtaining or providing biological samples comprising cell-free nucleic acids.	●*Id.*
13	Genotyping of a transplant donor and/or recipient could be performed by any suitable method known in the art by November 6, 2009, including sequencing, arrays, and PCR.	●B0001 at 7:23-28, 8:55-60, 9:8-14, 13:51-67, 14:58-67, 15:38-18:53, 20:30-34, 21:5-8, 26:47-52; ●Decl. ¶¶78-135 (citing further evidence).

14	After genotyping a transplant donor and recipient, using existing genotyping platforms known in the art by November 2009, one could identify approximately 1.2 million total genetic variations between a transplant donor and transplant recipient.	● B0001 at 5:36-49, 8:55-60, 9:8-14, 13:51-67, 13:58-64, 14:29-32, 14:58-67, 15:1-16:41, 16:50-17:28, 17:40-18:53, 20:31-44, 21:5-9, 23:31-36, 26:47-52; ● Decl. ¶¶78-135 (citing further evidence).
15	POSAs[1] prior to November 6, 2009, understood that usable SNPs for genotyping comprised approximately 500,000 heterozygous donor SNPs and approximately 160,000 homozygous donor SNPs. Companies offered both standard and custom-designed probe sets for SNP genotyping that could in principle target any desired SNP position for a PCR-based assay. POSAs could select a usable subset of existing or custom probes to serve as the probe set for a PCR-based assay for any donor/recipient pair.	● B0001-B0024 at 8:55-60, 9:8-14, 13:51-67, 14:29-67, 17:40-18:53; ● Decl. ¶¶78-92; ● B0086-B0093 at B0094, B0098-B0099, B0101, B0145, B0148; ● B0094-B0155; ● B0156-B0163 at B0159; ● B0164-B0183 at B0164; ● B0184-B0185; ● B0191-B0212 at B0196; ● B0213-B0223 at B0214; ● B0224-B0225 at B0224; ● B0226-B0243 at B0233; ● B0244-B0250 at B0248; ● B1291-B1300 at B1291

[1] "POSA" refers to a person of skill in the art defined in the Declaration of John Quackenbush, Ph.D. ("Decl."), ¶¶23-26.

16	Genotyping transplant donor and recipient nucleic acids, and/or detection, identification and/or quantification of the donor-specific nucleic acids (e.g. polymorphic markers such as SNPs) after transplantation could be performed by sequencing methods known in the art as of November 6, 2009.	● B0001 at 5:36-40, 6:16-19, 7:16-123, 7:30-46, 9:8-14,14:28-32, 15:1-8, 15:22-17:28, 21:5-8; ● Decl. ¶¶129-168 (citing further evidence)
17	The presence or absence of one or more nucleic acids from the transplant donor in the transplant recipient could be determined by any suitable method known in the art by November 6, 2009, including sequencing, nucleic acid arrays, and PCR.	● *Id.*
18	Laboratory instruments were commercially available by November 6, 2009 for multiplex or high-throughput sequencing of samples comprising cell-free nucleic acids.	● B0001 at 13:40-14:10, 15:1-16:8, 20:31-36; ● Decl. ¶¶93-121; ● B0260-B0263; ● B0251-B0259.
19	By 2008, established genomic analysis technologies included sequencing, next-	● B0581 at B0588;

	generation sequencing (also referred to as multiplex or high-throughput sequencing), and genotyping.	●B0001 at 5:36-4, 9:8-14, 13:58-64, 14:58-67, 15:1-17:31, 17:32-36, 20:31-36, 23:31-36, 26:47-52; ●Decl. ¶¶93-121 (citing further evidence).
20	By 2008, manufacturers of systems, supplies and reagents for performing genetic analysis, which includes DNA sequencing and genotyping, served a worldwide market of approximately $5 billion.	●B0581 at B0587; ●Decl. ¶71; ●B0587, B0589.
21	In a 10K SEC filing, Illumina reported that for 2007, its "[i]nstrument revenue increased by $77.6 million over prior year, of which $68.7 million was due to increased sales of our sequencing systems, particularly the Genome Analyzer and cluster stations." For 2008, Illumina reported that its "[i]nstrument revenue increased to $64.8 million over prior year, of which $63.0 million was due to increased sales of [its] sequencing systems" and that "[t]his increase in revenue can be primarily attributed to shipments of our second generation Genome Analyzer, the Genome Analyzer II."	●Decl. ¶105; ●B0927, B0935, B940.
22	By November 6, 2009, commercially available machines were used by POSAs to perform multiplex or high-throughput sequencing, including shotgun sequencing, to detect and quantify SNPs.	●B0001 at 9:8-14, 15:1-16:41; 16:50-17:39, 26:47-52; ●Decl. ¶¶99-113 (citing further evidence).
23	Neither the written description nor the claims of the Patents disclose	●B0001 at 5:36-40; 7:23-28, 8:55-60, 9:8-

	nonconventional techniques for performing genotyping and/or multiplex / high-throughput sequencing, individually or in combination.	14, 13:51-67, 14:58-67, 15: 12-18, 15:38-46, 15:53-17:36, 17:40-18:53, 20:30-34, 21:5-8, 26:47-53; ● B0025; ● B0049; ● Decl. ¶¶78-135; 146-169, 178-188, 198-199 (citing further evidence).
24	Quantitation of donor-specific DNA(e.g., polymorphic markers such as SNPs) could be performed using real-time PCR, chips, or high-throughput shotgun sequencing of cell-free nucleic acids, as well as other methods known in the art, by November 6, 2009.	● B0001 at 5:36-40, 9:8-14, 14:29-32, 15:2-17:28, 21:5-9; ● Decl. ¶¶124-135; ● B0360-B0362; ● B0224-B0025; ● B0226-B0243.
25	The Patents do not disclose or claim any nonconventional laboratory techniques for achieving sensitivity of a method for detecting transplant rejection, graft dysfunction, or organ failure that is greater than 56% compared to sensitivity of current surveillance methods for cardiac allograft vasculopathy (CAV) as of November 6, 2009 or how that sensitivity may be achieved.	● B0001 at 5:36-49, 16:20-59, 17:1-28, 23:31-44; ● Decl. ¶¶114-122; ● B0236; ● B0357; ● B1301.
26	POSAs understood before November 6, 2009 that using sequencing, there are two components to sensitivity: (i) the number of molecules analyzed (depth of sequencing) and (ii) the error rate of the sequencing process.	● *Id.*

27	POSAs understood before November 6, 2009 that higher sensitivity can be achieved by sequencing more molecules.	• *Id.*
28	POSAs understood before November 6, 2009 that it is possible to systematically lower the sequencing error rate by resequencing the sample template multiple times.	• *Id.*
29	The Patents do not disclose or claim any nonconventional ways to achieve higher sensitivities and lower error rates using the sequencing equipment commercially available as of November 6, 2009.	• *Id.*

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Dated: June 11, 2020

CERTIFICATE OF COMPLIANCE

Pursuant to the Court's November 6, 2019 Standing Order, I hereby confirm that this brief complies with the type and number limitations set forth in the Standing Order. I certify that this document contains 1,686 words, which were counted using the word count feature in Microsoft Word, in 14-point Times New Roman font. The word count does not include the cover page or the counsel blocks.

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